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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/801,540	03/08/2001	Adrian Bot	A30571-A-PCT/USA-A	7183

7590 12/18/2007

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EXAMINER	
SGAGIAS, MAGDALENE K	
ART UNIT	**PAPER NUMBER**
1632	

MAIL DATE	DELIVERY MODE
12/18/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/801,540	BOT ET AL.	
	Examiner	Art Unit	
	Magdalene K. Sgagias	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 2* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/31/07 has been entered.

Applicant's arguments filed 10/31/07 have been fully considered but they are not persuasive. The amendment has been entered. Claims 1-2 are pending and under consideration. Claim 3 has been canceled.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Assateerawatt et al, (Asian Pacitic Journal of Allergy and Immunology, 11: 85-91, 1993 (IDS)) in view of Donnely et al, (Journal of Immunological Methods, 176: 145-152, 1994 (IDS)).

Assateerawatt et al, teach the immunogenicity and efficacy of of a recombinant DNA Hepattis B vaccine, GenHevac B Pasteur in high risk neonates born from HBsAg and HBeAg positive mothers, school children and healthy adults (title). Assateerawatt et al, teach the inoculation of infants "group B" with hepatitis B protein antigens using the recombinat hepatitis B

vaccine, GeneHevac B Pasteur, containing pre S1, pre S2 and S proteins at birth, 1, 2 and 12 months of age (p 86, 1st column, lines 1-8, and 2nd column, abstract)). Assateerawatt et al, teach also the inoculation of infants 'group B) with the hepatitis B immunoglobulin (HBIG) (p 86, 2nd column). Assateerawatt et al, teach the protective efficacy of gorup A and B were 95.5% and 89.8% respectively, with no statistical significant difference (abstract). Assateerawatt et al, teach the antibody titer declined gradually in both groups (p 87, 3rd column bridge to p 88). Assateerawatt et al, also discusses a very important probelm in the control and especially te helimination of hepatitis B virus is the duration of immunity and the necessity to booster immunization (p 90, 2nd column last paragraph). Assateerawatt et al, differs from the present invention for not teaching a naked DNA hepatitis vaccine.

However, at the time of the present invention Donnelly et al, teach immunization with naked DNA which induces both antibody and cell-mediated immune response which can serve as an alterantive to immunization with attenuated viruses (abstract and entire document). Donnelly discuses methods for inducing immune responses with DNA including hepatitis B virus surface antigen (HBsAg) (p 147, 2nd column last pragraph bridge to p 148). Donnelly concludes immunization with DNA is a simple, robust and effective means of eliciting both antibody and cell-mediated immune responses against viral proteins that is at least equivalent to that produced by immunization with conventional methods (p 150, 2nd column under conclusion). As such, Donnely provides sufficient motivation for one ordinary skil in the art to apply a DNA hepatitis B virus surface antigen (HBsAg) vaccine in the neonates of Assateerawatt et al.

Accordingly, in view of the teachings of Donnelly et al, it would have been obvious for one of ordinary skill in the art, at the time the claimed invention was made, to apply a DNA hepatitis B virus surface antigen (Bag) in a neonates at birth or 1 month of high risk neonates

born from HBsAg positive mothers with a reasonable expectation of success. One of ordinary skill in the art would have been sufficiently motivated to make such a modification as Donnelly concludes immunization with DNA is a simple, robust and effective means of eliciting both antibody and cell-mediated immune responses against viral proteins that is at least equivalent to that produced by immunization with conventional methods.

Thus, the claimed invention as a whole, is clearly prima facie obvious in the absence of evidence to the contrary.

Claims 1-2 are rejected under 35 U.S.C. 103(a) as being unpatentable over Assateerawatt et al, (Asian Pacitic Journal of Allergy and Immunology, 11: 85-91, 1993 (IDS)) in view of Donnelly et al, (Journal of Immunological Methods, 176: 145-152, 1994 (IDS)) and further in view of **Chisari et al,** (Springer Semin Immunopathol, 17: 261-282, 1995).

The 103 rejection of claim 1 as being unpatentable over Assateerawatt et al, taken with Donnelly et al, is applied as indicated above.

Assateerawatt et al, taken with Donnelly et al, do not teach an inclusion of more than one relevant epitope of one or more target antigens associated with the pathogen.

However, at the time of the present invention **Chisari et al,** teach clonal deletion of HBV-specific T cells as a consequence of transplacental infection of the developing fetus, or transplacental passage of sub viral antigens could play an important role in the chronic infection that develops in neonates born to infected mothers (p 271, under neonatal tolerance). Alternatively, postnatal infection may induce a weak and defective HBV-specific immune response because of the immunological immaturity of the newborn infant, although this is less

attractive since it is well known that newborn infants respond quite well to immunization with **HBsAg**. Therefore, it is likely that transplacental infection or passage of soluble and/or particulate viral antigens contribute substantially to viral persistence in the infected neonate. In line with this possibility, it has been shown that nontransgenic progeny of **HBeAg**-positive transgenic mothers are tolerant to both HBeAg and HBcAg at the T cell level, presumably due to the thymic deletion of MHC class II-restricted HBV nucleocapsid-specific helper T cells as a result of transplacental exposure to HBeAg. Since intrauterine infection of the fetal liver by HBV has been described by many investigators, it is likely that not only tolerance to HBV nucleocapsid antigens but also to the other viral proteins can contribute to viral persistence by negative selection of the responding cells in the thymus during fetal development. Interestingly, neonates born to HBeAg-positive mothers are effectively protected against HBV infection when immunized with the HBsAg vaccine even though their immune system may have been exposed to HBV envelope antigens during its maturation. This suggests that neonates are immunocompetent with respect to this (HBsAg) antigen and that HBV envelope-specific T and B cells are still present and functional. This may indicate that tolerance to HBV envelope antigens is not induced in this setting or that exposure to viral proteins during fetal life does not result in a permanent state of tolerance if non-responsiveness can be reversed by HBsAg immunization (p 271, under neonatal tolerance). As such, Chisari et al provide sufficient motivation for one of ordinary skill in the art to apply the HBeAg to the HBsAg DNA vaccine of Assateerawatt et al and Donnelly et al.

Accordingly, in view of the teachings of Chisari et al, it would have been obvious for one of ordinary skill in the art, at the time the claimed invention was made, to modify the HBsAg DNA vaccine of Assateerawatt et al and Donnelly et al by use of HBeAg relevant epitope for inducing a T cell response in high risk neonates born from HBsAg and HBeAg positive mothers,

with a reasonable expectation of success. One of ordinary skill in the art would have been sufficiently motivated to make such a modification as Chisari et al suggests that neonates born to HBeAg-positive mothers are effectively protected against HBV infection when immunized with the HBsAg vaccine and that HBV envelope-specific T and B cells are still present and functional, particularly since Assateerawatt et al, noted that infants serum samples of the vaccinated neoantes tested for HBsAg antibody titer declined gradually by use of the protein vaccine and moreover since Donnelly teaches that DNA vaccines induce both humoral and cellular immune response.

Thus, the claimed invention as a whole, is clearly prima facie obvious in the absence of evidence to the contrary.

Applicant's arguments are moot in view of the new rejections.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 1 and 2 rejection under 35 U.S.C. 101 as claiming the same invention as that of claims 1-47 of copending Application No. 10/351,630 is withdrawn.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Magdalene K. Sgagias whose telephone number is (571) 272-3305. The examiner can normally be reached on Monday through Friday from 9:00 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, Jr., can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Magdalene K. Sgagias, Ph.D.
Art Unit 1632

/Anne-Marie Falk/
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Primary Examiner, Art Unit 1632